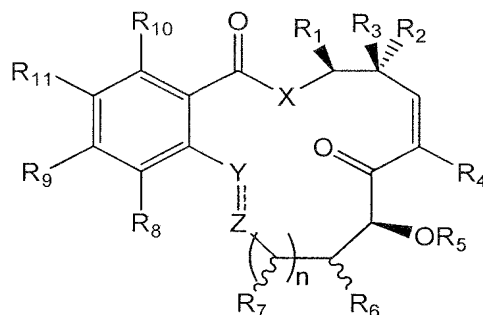


AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listing of claims in the application.

Listing of Claims

1. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester thereof; wherein

R₁ is hydrogen, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀ heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀ heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl or C₃-C₁₄ heteroaryl;

R₂ is methyl;

R₃ is hydrogen or halogen;

R₄ is hydrogen or halogen;

R₅ is hydrogen or an oxygen protecting group;

R₆ is hydrogen, hydroxyl, or ~~protected hydroxyl~~ with an oxygen protecting group;

n is 0-2 1;

R₇ is hydrogen;

R₈ is hydrogen, halogen, hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, or alkyloxy;

R₉ is hydrogen, halogen, hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, OR₁₂, SR₁₂, NR₁₂R₁₃, -X₁(CH₂)_pX₂-R₁₄, or is lower alkyl optionally substituted with hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, C_2 - C_{20} alkynyl, C_1 - C_{20} heteroalkyl, C_2 - C_{20} heteroalkenyl, C_2 - C_{20} heteroalkynyl, C_3 - C_{20} cycloalkyl, C_3 - C_{20} cycloalkenyl, C_3 - C_{20} cycloalkynyl, C_3 - C_{20} heterocycloalkyl, C_3 - C_{20} heterocycloalkenyl, C_3 - C_{20} heterocycloalkynyl, C_3 - C_{14} aryl or C_3 - C_{14} heteroaryl; or a nitrogen or oxygen protecting group, or R_{12} and R_{13} , taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, protected hydroxyl with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2 - R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety;

p is 2-10, and

R_{14} is hydrogen, or a C_3 - C_{14} aryl, C_3 - C_{14} heteroaryl, C_1 - C_{20} alkyl(C_3 - C_{14})aryl, or C_1 - C_{20} alkyl(C_3 - C_{14})heteroaryl moiety, or is $-(C=O)NHR_{15}$, $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl, C_2 - C_{20} alkynyl, C_1 - C_{20} heteroalkyl, C_2 - C_{20} heteroalkenyl, C_2 - C_{20} heteroalkynyl, C_3 - C_{20} cycloalkyl, C_3 - C_{20} cycloalkenyl, C_3 - C_{20} cycloalkynyl, C_3 - C_{20} heterocycloalkyl, C_3 - C_{20} heterocycloalkenyl, C_3 - C_{20} heterocycloalkynyl, C_3 - C_{14} aryl or C_3 - C_{14} heteroaryl; or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is a C_1 - C_{20} alkyl, C_2 - C_{20} alkenyl or C_2 - C_{20} alkynyl moiety, wherein one or more of R_{14} , R_{15} , or R_{16} are optionally substituted with one or more occurrences of hydroxyl, protected hydroxyl with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

~~R_8 and R_9 may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;~~

R_{10} is hydroxyl, protected hydroxyl with an oxygen protecting group, or amino;

R_{11} is hydrogen;

X is O;

Y is CHR_{17} or CR_{17} ; and Z is CHR_{18} or CR_{18} ;

wherein each occurrence of R_{17} and R_{18} is hydrogen and wherein Y and Z may be connected by a single or double bond;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyl dimethylsilyl ether, tribenzyl silyl ether, t-butyl diphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, ~~Free~~ 2,2,2-trichloroethoxycarbonyl, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

wherein $\text{C}_3\text{-C}_{14}$ heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

2. (currently amended) The composition of claim 1, wherein:

R_1 is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or $\text{C}_3\text{-C}_{14}$ aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more ~~occurrences of~~ halogen, hydroxyl or ~~protected~~ hydroxyl with an oxygen protecting group;

R_3 is hydrogen;

R_9 is hydrogen, halogen, hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, OR_{12} , SR_{12} , $\text{NR}_{12}\text{R}_{13}$,

$-\text{X}_1(\text{CH}_2)_p\text{X}_2\text{-R}_{14}$, or is lower alkyl optionally substituted with hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, halogen, amino, protected amino, or $-\text{X}_1(\text{CH}_2)_p\text{X}_2\text{-R}_{14}$;

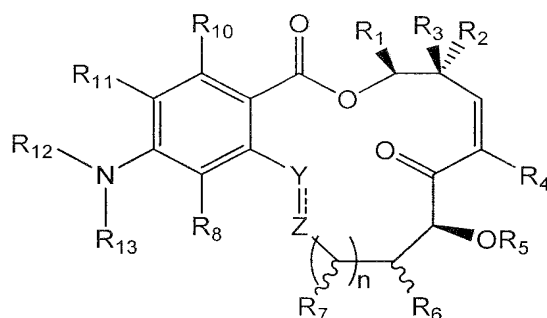
wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, lower alkyl, $\text{C}_3\text{-C}_{14}$ aryl, $\text{C}_3\text{-C}_{14}$ heteroaryl, alkyl($\text{C}_3\text{-C}_{14}$)aryl, or alkyl($\text{C}_3\text{-C}_{14}$)heteroaryl, or a nitrogen or oxygen protecting group, or R_{12} and R_{13} , taken together may form a

saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen, wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or -N(alkyl), or wherein X_2 - R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety, p is 2-10, and

R_{14} is hydrogen, or a C_3 - C_{14} aryl, C_3 - C_{14} heteroaryl, alkyl(C_3 - C_{14})aryl, or alkyl(C_3 - C_{14})heteroaryl moiety, or is $-(C=O)NHR_{15}$, $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, C_3 - C_{14} aryl, C_3 - C_{14} heteroaryl, alkyl(C_3 - C_{14})aryl, or alkyl(C_3 - C_{14})heteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14} , R_{15} , or R_{16} are optionally substituted with one or more occurrences of hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; and R_{10} is hydroxyl.

3. (canceled)
4. (original) The composition of claim 2, where R_4 is halogen.
5. (currently amended) The composition of claim 2, where R_4 is ~~fluorine~~ hydrogen.
6. (original) The composition of claim 2, where Y and Z together represent $-CH=CH-$.
7. (original) The composition of claim 2, where Y and Z together represent trans $-CH=CH-$.
8. (previously presented) The composition of claim 2, wherein R_1 is methyl.
9. (canceled)
10. (original) The composition of claim 8, wherein R_4 is halogen.
11. (original) The composition of claim 8, wherein Y and Z together represent $-CH=CH-$.

12. (currently amended) The composition of claim 8, wherein ~~n is 1~~, R₄ is ~~halogen~~ hydrogen and Y and Z together represent -CH=CH-.
13. (original) The composition of claim 11 or 12 wherein -CH=CH- is trans.
14. (currently amended) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester thereof; wherein

R₁ is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C₃-C₁₄ aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more ~~occurrences of~~ halogen, hydroxyl protected hydroxyl with an oxygen protecting group;

R₂ is methyl;

R₃ is hydrogen or halogen;

R₄ is hydrogen or halogen;

R₅ is hydrogen or an oxygen protecting group;

R₆ is hydrogen, hydroxyl, or ~~protected~~ hydroxyl with an oxygen protecting group;

n is 0-2 1;

R₇ is hydrogen;

R₈ is hydrogen, halogen, hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, or alkyloxy;

R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, lower alkyl, C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl, or a nitrogen or oxygen protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated

cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more occurrences of hydroxyl, ~~protected hydroxyl with an oxygen protecting group~~, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R_{10} is hydroxyl, ~~protected hydroxyl with an oxygen protecting group~~, or amino;

R_{11} is hydrogen;

Y is CHR_{17} or CR_{17} ; and Z is CHR_{18} or CR_{18} ;

wherein each occurrence of R_{17} and R_{18} is hydrogen wherein Y and Z may be connected by a single or double bond, ~~or~~

~~R_{13} and R_8 may, when taken together, form a cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen;~~

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, ~~Free~~ 2,2,2-trichloroethoxycarbonyl, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

wherein C_3 - C_{14} heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

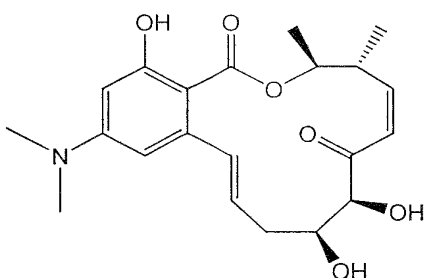
15. (canceled)
16. (original) The composition of claim 14, wherein R_4 is halogen.
17. (original) The composition of claim 14, wherein Y and Z together represent $-CH=CH-$.
18. (previously presented) The composition of claim 14, wherein R_1 is methyl.

19. (currently amended) The composition of claim 14, wherein ~~n is 1~~, R₁ is methyl, R₄ is ~~halogen~~ hydrogen, and Y and Z together represent -CH=CH-.

20. (original) The composition of claim 17 or 19, wherein -CH=CH- is trans.

21-22. (canceled)

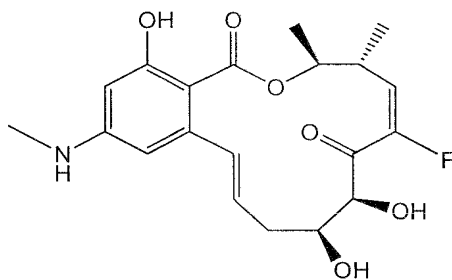
23. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

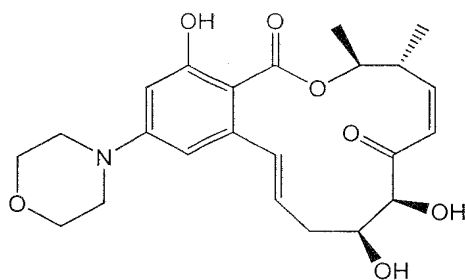
24-26. (canceled)

27. (previously presented) The composition of claim 14, wherein the compound has the structure:



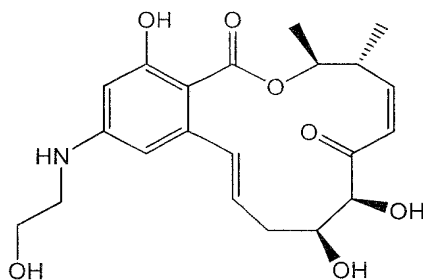
or a pharmaceutically acceptable salt or ester thereof.

28. (previously presented) The composition of claim 14, wherein the compound has the structure:



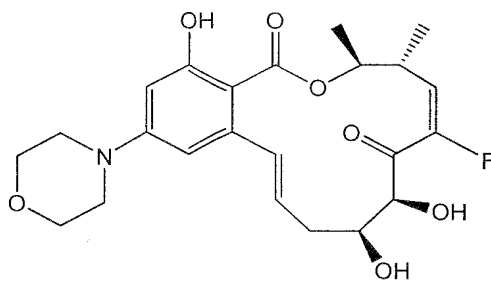
or a pharmaceutically acceptable salt or ester thereof.

29. (previously presented) The composition of claim 14, wherein the compound has the structure:



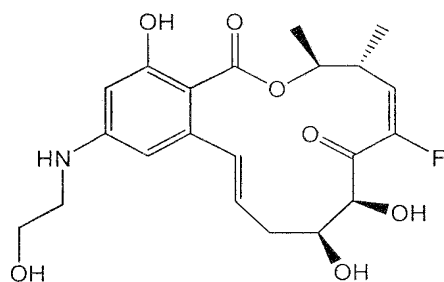
or a pharmaceutically acceptable salt or ester thereof.

30. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

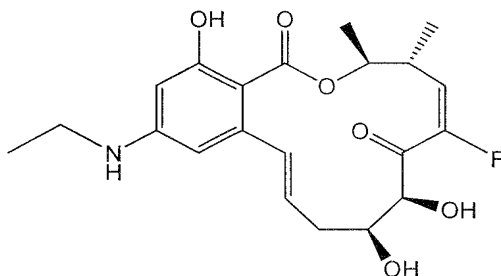
31. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

32. (canceled)

33. (previously presented) The composition of claim 14, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

34-45. (canceled)

46. (withdrawn, currently amended) The composition of claim 2, where R_1 is hydrogen methyl.

47. (withdrawn, currently amended) The composition of claim [[1]] 2, where [[R₃]] R₄ is halogen.

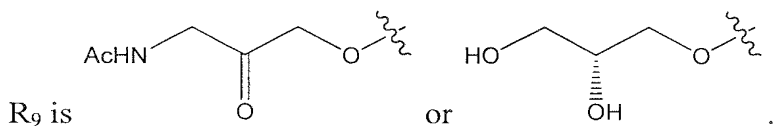
48. (withdrawn) The composition of claim 2, where R_4 is hydrogen.

49. (withdrawn) The composition of claim 2, where R_5 is hydrogen.

50. (withdrawn) The composition of claim 2, where R_6 is hydroxyl.

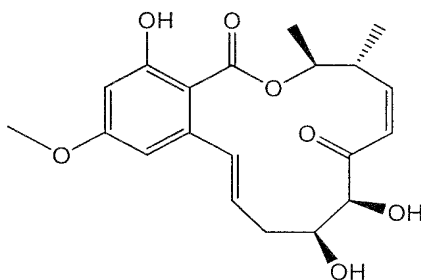
51. (canceled)

52. (withdrawn, currently amended) The composition of claim 1, where R_8 is ~~halogen~~ hydrogen.
53. (withdrawn, currently amended) The composition of claim 2, where R_9 is hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, $-OR_{12}$, $-NR_{12}R_{13}$, or $-O(CH_2)_pX_2$, R_{14} , wherein R_{12} , R_{13} , R_{14} and X_2 are as defined in claim 2.
54. (withdrawn, currently amended) The composition of claim 53, where R_9 is $-OR_{12}$, wherein R_{12} is methyl, ethyl, propyl, isopropyl, butyl, ~~[[Bn]]~~ benzyl, ~~PMB (MPM)~~ para-methoxybenzyl, ~~3,4-ClBn~~ 3,4-dichlorobenzyl, or



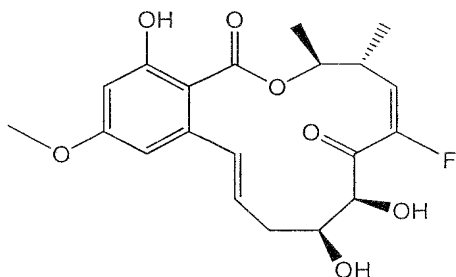
55.-61. (canceled)

62. (previously presented) The composition of claim 1 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

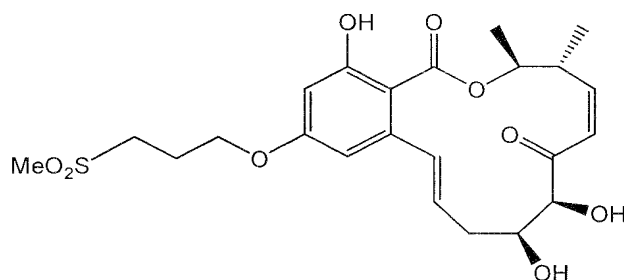
63. (previously presented) The composition of claim 1 wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

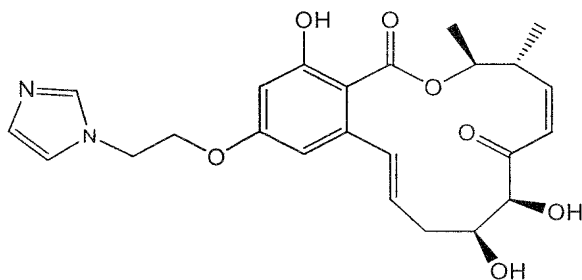
64. (canceled)

65. (previously presented) The composition of claim 1 wherein the compound has the structure:



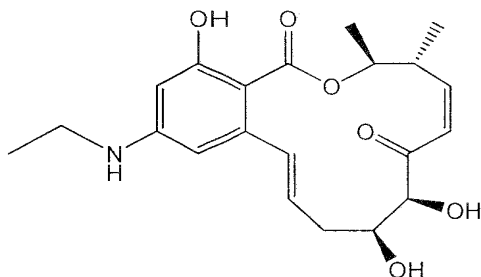
or a pharmaceutically acceptable salt or ester thereof.

66. (previously presented) The composition of claim 1 wherein the compound has the structure:



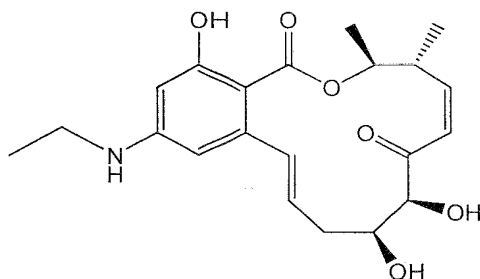
or a pharmaceutically acceptable salt or ester thereof.

67. (previously presented) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:

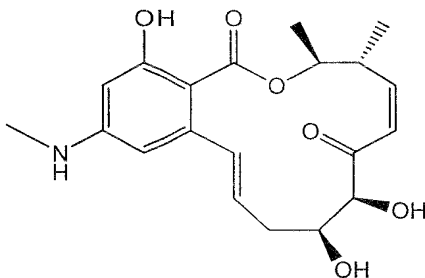


or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

68. (currently amended) The composition of claim 67, ~~having the structure~~ wherein the compound is:

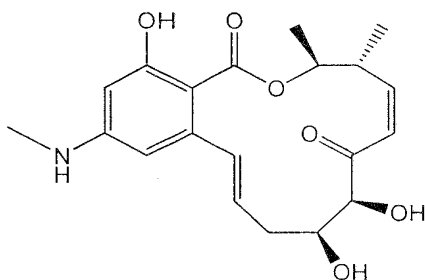


69. (previously presented) A pharmaceutical composition for systemic administration comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:

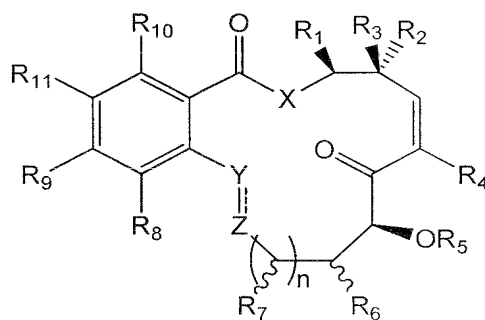


or a pharmaceutically acceptable salt, ester, or salt of ester thereof.

70. (currently amended) The composition of claim 69, having the structure wherein the
compound is:



71. (previously presented) The composition of claim 2, wherein R₄, R₅ and R₈ are hydrogen, R₆ and R₁₀ are hydroxyl, and Y and Z together represent trans -CH=CH-.
72. (previously presented) The composition of claim 71, wherein R₁ is methyl.
73. (previously presented) The composition of claim 14, wherein R₄, R₅ and R₈ are hydrogen, R₆ and R₁₀ are hydroxyl, and Y and Z together represent trans -CH=CH-.
74. (previously presented) The composition of claim 73, wherein R₁ is methyl.
75. (currently amended) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester or salt of ester thereof; wherein R₁ is hydrogen, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀ heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀ heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl or C₃-C₁₄ heteroaryl;

R₂ is methyl;

R₃ is hydrogen or halogen;

R₄ is hydrogen or halogen;

R₅ is hydrogen or an oxygen protecting group;

R₆ is hydrogen, hydroxyl, or ~~protected~~ hydroxyl with an oxygen protecting group;

n is ~~0-2~~ 1;

R₇ is hydrogen;

R₈ is hydrogen, halogen, hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, or alkyloxy;

R₉ is hydrogen, halogen, hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, OR₁₂, SR₁₂, NR₁₂R₁₃,

-X₁(CH₂)_pX₂-R₁₄, or is lower alkyl optionally substituted with hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, halogen, amino, protected amino, or -X₁(CH₂)_pX₂-R₁₄;

wherein R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀ heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀ heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl or C₃-C₁₄ heteroaryl; or a nitrogen or oxygen protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more ~~occurrences of~~ hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X₁ and X₂ are each independently absent, or are oxygen, NH, or

-N(alkyl), or wherein X₂-R₁₄ together are N₃ or are a saturated or unsaturated heterocyclic moiety;

p is 2-10, and

R₁₄ is hydrogen or a C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, C₁-C₂₀ alkyl(C₃-C₁₄)aryl, or C₁-C₂₀ alkyl(C₃-C₁₄)heteroaryl moiety, or is -(C=O)NHR₁₅, -(C=O)OR₁₅, or -(C=O)R₁₅, wherein each occurrence of R₁₅ is independently hydrogen, C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl, C₂-C₂₀ alkynyl, C₁-C₂₀ heteroalkyl, C₂-C₂₀ heteroalkenyl, C₂-C₂₀

heteroalkynyl, C₃-C₂₀ cycloalkyl, C₃-C₂₀ cycloalkenyl, C₃-C₂₀ cycloalkynyl, C₃-C₂₀ heterocycloalkyl, C₃-C₂₀ heterocycloalkenyl, C₃-C₂₀ heterocycloalkynyl, C₃-C₁₄ aryl or C₃-C₁₄ heteroaryl; or R₁₄ is -SO₂(R₁₆), wherein R₁₆ is a C₁-C₂₀ alkyl, C₂-C₂₀ alkenyl or C₂-C₂₀ alkynyl moiety, wherein one or more of R₁₄, R₁₅, or R₁₆ are optionally substituted with one or more occurrences of hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; or

~~R₈ and R₉ may, when taken together, form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydroxyl, protected hydroxyl, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;~~

R₁₀ is hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, or amino;

R₁₁ is hydrogen;

X is O;

Y is CHR₁₇ or CR₁₇; and Z is CHR₁₈ or CR₁₈;

wherein each occurrence of R₁₇ and R₁₈ is hydrogen and wherein Y and Z may be connected by a single or double bond;

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl ether, triethylsilyl ether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, ~~Free~~ 2,2,2-trichloroethoxycarbonyl, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

wherein C₃-C₁₄ heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

76. (currently amended) The composition of claim 75, wherein:

R_1 is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C_3 - C_{14} aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more ~~occurrences of~~ halogen, hydroxyl or protected hydroxyl with an oxygen protecting group;

R_3 is hydrogen;

R_8 is hydrogen;

R_9 is hydrogen, halogen, hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, OR_{12} , SR_{12} , $NR_{12}R_{13}$,

$-X_1(CH_2)_pX_2-R_{14}$, or is lower alkyl optionally substituted with hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, halogen, amino, protected amino, or $-X_1(CH_2)_pX_2-R_{14}$;

wherein R_{12} and R_{13} are, independently for each occurrence, hydrogen, lower alkyl, C_3 - C_{14} aryl, C_3 - C_{14} heteroaryl, alkyl(C_3 - C_{14})aryl, or alkyl(C_3 - C_{14})heteroaryl, or a nitrogen or oxygen protecting group, or R_{12} and R_{13} , taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R_{12} and R_{13} are optionally further substituted with one or more ~~occurrences of~~ hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen,

wherein X_1 and X_2 are each independently absent, or are oxygen, NH, or $-N(\text{alkyl})$, or

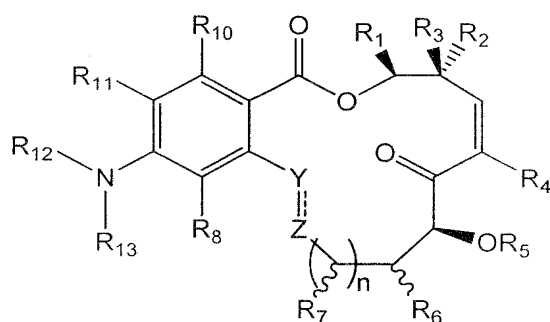
wherein X_2-R_{14} together are N_3 or are a saturated or unsaturated heterocyclic moiety,

p is 2-10, and

R_{14} is hydrogen, or a C_3 - C_{14} aryl, C_3 - C_{14} heteroaryl, alkyl(C_3 - C_{14})aryl, or alkyl(C_3 - C_{14})heteroaryl moiety, or is $-(C=O)NHR_{15}$, $-(C=O)OR_{15}$, or $-(C=O)R_{15}$, wherein each occurrence of R_{15} is independently hydrogen, alkyl, heteroalkyl, C_3 - C_{14} aryl, C_3 - C_{14} heteroaryl, alkyl(C_3 - C_{14})aryl, or alkyl(C_3 - C_{14})heteroaryl, or R_{14} is $-SO_2(R_{16})$, wherein R_{16} is an alkyl moiety, wherein one or more of R_{14} , R_{15} , or R_{16} are optionally substituted with one or more ~~occurrences of~~ hydroxyl, ~~protected hydroxyl~~ with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen; and R_{10} is hydroxyl.

77. (canceled)

78. (previously presented) The composition of claim 76, where R_4 is halogen.
79. (currently amended) The composition of claim 76, where R_4 is ~~fluorine~~ hydrogen.
80. (previously presented) The composition of claim 76, where Y and Z together represent $-\text{CH}=\text{CH}-$.
81. (previously presented) The composition of claim 76, where Y and Z together represent trans $-\text{CH}=\text{CH}-$.
82. (previously presented) The composition of claim 76, wherein R_1 is methyl.
83. (canceled)
84. (previously presented) The composition of claim 82, wherein R_4 is halogen.
85. (previously presented) The composition of claim 82, wherein Y and Z together represent $-\text{CH}=\text{CH}-$.
86. (currently amended) The composition of claim 82, wherein ~~n is 1~~, R_4 is ~~halogen~~ hydrogen and Y and Z together represent $-\text{CH}=\text{CH}-$.
87. (previously presented) The composition of claim 85 or 86 wherein $-\text{CH}=\text{CH}-$ is trans.
88. (currently amended) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



or a pharmaceutically acceptable salt or ester or salt of ester thereof; wherein

R₁ is hydrogen, straight or branched lower alkyl, straight or branched lower heteroalkyl, or C₃-C₁₄ aryl,

wherein the alkyl, heteroalkyl, and aryl groups may optionally be substituted with one or more occurrences of halogen, hydroxyl or ~~protected~~ hydroxyl with an oxygen protecting group;

R₂ is methyl;

R₃ is hydrogen or halogen;

R₄ is hydrogen or halogen;

R₅ is hydrogen or an oxygen protecting group;

R₆ is hydrogen, hydroxyl, or ~~protected~~ hydroxyl with an oxygen protecting group;

n is ~~0-2~~ 1;

R₇ is hydrogen;

R₈ is hydrogen, halogen, hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, or alkyloxy;

R₁₂ and R₁₃ are, independently for each occurrence, hydrogen, lower alkyl, C₃-C₁₄ aryl, C₃-C₁₄ heteroaryl, alkyl(C₃-C₁₄)aryl, or alkyl(C₃-C₁₄)heteroaryl, or a nitrogen or oxygen protecting group, or R₁₂ and R₁₃, taken together may form a saturated or unsaturated cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms, and each of R₁₂ and R₁₃ are optionally further substituted with one or more occurrences of hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, alkyloxy, amino, protected amino, alkylamino, aminoalkyl, or halogen;

R₁₀ is hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, or amino;

R₁₁ is hydrogen;

Y is CHR₁₇ or CR₁₇; and Z is CHR₁₈ or CR₁₈;

wherein each occurrence of R₁₇ and R₁₈ is hydrogen, wherein Y and Z may be connected by a single or double bond, or

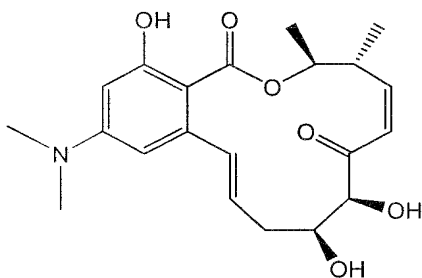
~~R₁₃ and R₈ may, when taken together, form a cyclic ring of 1 to 4 carbon atoms and 1 to 3 nitrogen or oxygen atoms and is optionally substituted with hydrogen, alkyloxy, amino, alkylamino, aminoalkyl, and halogen;~~

wherein oxygen protecting groups are selected from the group consisting of methyl ethers, methoxymethyl ether, methylthiomethyl ether, benzyloxymethyl ether, p-methoxybenzyloxymethyl ether, ethyl ethers, benzyl ethers, silyl ethers, trimethylsilyl

ether, triethylsilylether, triisopropylsilyl ether, t-butyldimethylsilyl ether, tribenzyl silyl ether, t-butyldiphenyl silyl ether, esters, formate, acetate, benzoate, trifluoroacetate, dichloroacetate, carbonates, cyclic acetals and ketals and wherein nitrogen protecting groups are selected from the group consisting of carbamates, ~~Free~~ 2,2,2-trichloroethoxycarbonyl, amides, cyclic imides, N-alkyl amines, N-aryl amines, imines, and enamines; and

wherein C₃-C₁₄ heteroaryl moieties are selected from cyclic aromatic moieties having from five to ten ring atoms of which one ring atom is selected from S, O and N; zero, one or two ring atoms are additional heteroatoms independently selected from S, O and N; and the remaining ring atoms are carbon.

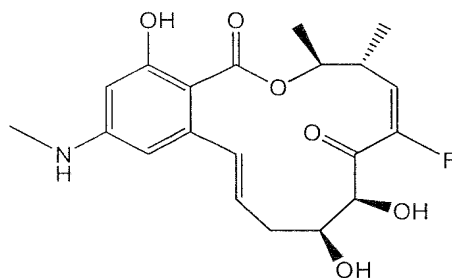
89. (canceled)
90. (previously presented) The composition of claim 88, wherein R₄ is halogen.
91. (previously presented) The composition of claim 88, wherein Y and Z together represent -CH=CH-.
92. (previously presented) The composition of claim 88, wherein R₁ is methyl.
93. (currently amended) The composition of claim 88, wherein ~~n is 1~~, R₁ is methyl, R₄ is ~~halogen~~ hydrogen, and Y and Z together represent -CH=CH-.
94. (previously presented) The composition of claim 91 or 93, wherein -CH=CH- is trans.
95. (previously presented) The composition of claim 88, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

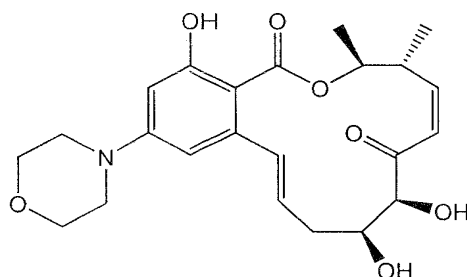
96. (canceled)

97. (previously presented) The composition of claim 88, wherein the compound has the structure:



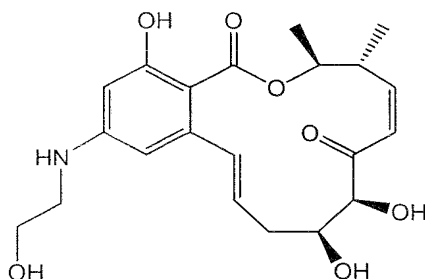
or a pharmaceutically acceptable salt or ester thereof.

98. (previously presented) The composition of claim 88, wherein the compound has the structure:



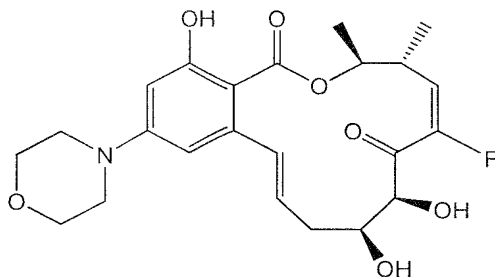
or a pharmaceutically acceptable salt or ester thereof.

99. (previously presented) The composition of claim 88, wherein the compound has the structure:



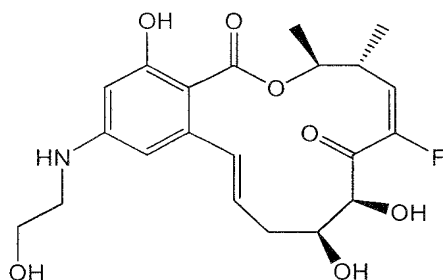
or a pharmaceutically acceptable salt or ester thereof.

100. (previously presented) The composition of claim 88, wherein the compound has the structure:



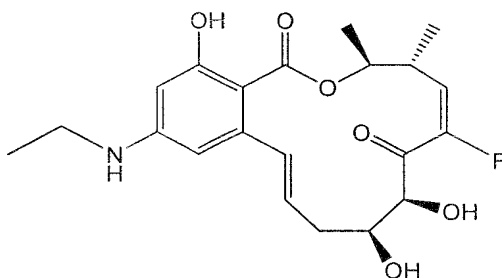
or a pharmaceutically acceptable salt or ester thereof.

101. (previously presented) The composition of claim 88, wherein the compound has the structure:



or a pharmaceutically acceptable salt or ester thereof.

102. (previously presented) The composition of claim 88, wherein the compound has the structure:

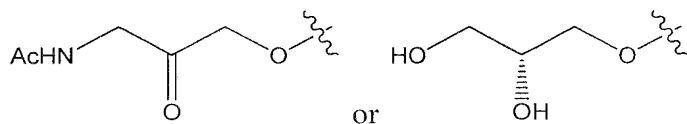


or a pharmaceutically acceptable salt or ester thereof.

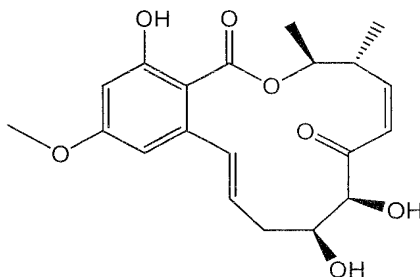
103. (currently amended) The composition of claim 76, where R_1 is ~~hydrogen~~ methyl.

104. (currently amended) The composition of claim ~~[[75]]~~ 76, where ~~[[R₃]]~~ R₄ is halogen.

105. (previously presented) The composition of claim 76, where R_4 is hydrogen.
106. (previously presented) The composition of claim 76, where R_5 is hydrogen.
107. (previously presented) The composition of claim 76, where R_6 is hydroxyl.
108. (currently amended) The composition of claim 75, where R_8 is ~~halogen~~ hydrogen.
109. (currently amended) The composition of claim 76, where R_9 is hydroxyl, ~~protected~~ hydroxyl with an oxygen protecting group, $-OR_{12}$, $-NR_{12}R_{13}$, or $-O(CH_2)_pX_2-R_{14}$, wherein R_{12} , R_{13} , R_{14} and X_2 are as defined in claim 76.
110. (currently amended) The composition of claim 109, where R_9 is $-OR_{12}$, wherein R_{12} is methyl, ethyl, propyl, isopropyl, butyl, ~~[[Bn]]~~ benzyl, ~~PMB (MPM)~~ para-methoxybenzyl, ~~3,4-ClBn~~ 3,4-dichlorobenzyl, or R_9 is

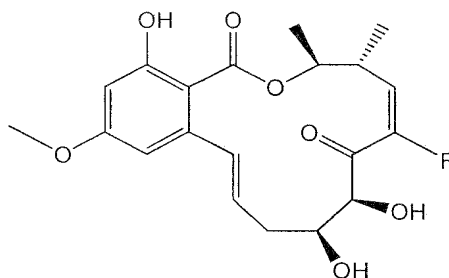


111. (previously presented) The composition of claim 75 wherein the compound has the structure:



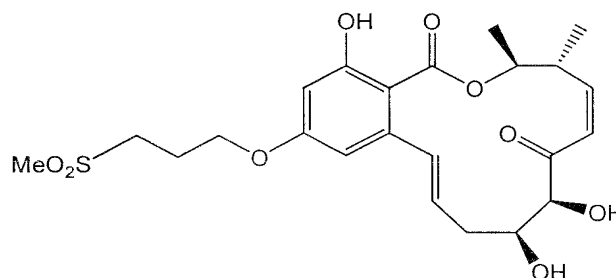
or a pharmaceutically acceptable salt or ester thereof.

112. (previously presented) The composition of claim 75 wherein the compound has the structure:



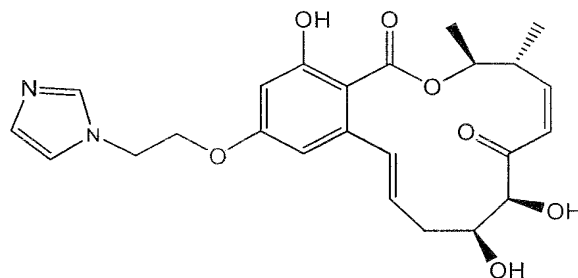
or a pharmaceutically acceptable salt or ester thereof.

113. (previously presented) The composition of claim 75 wherein the compound has the structure:



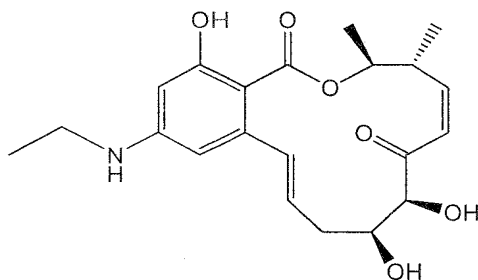
or a pharmaceutically acceptable salt or ester thereof.

114. (previously presented) The composition of claim 75 wherein the compound has the structure:

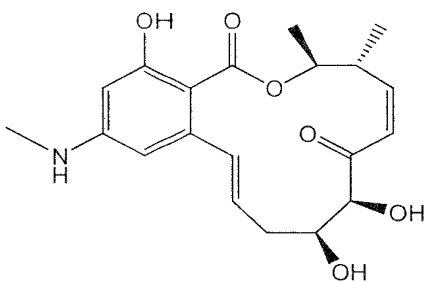


or a pharmaceutically acceptable salt or ester thereof.

115. (previously presented) A pharmaceutical composition comprising a pharmaceutically suitable carrier or diluent and a compound having the structure:



118. (currently amended) The composition of claim 117, ~~having the structure~~ wherein the compound is:



119. (previously presented) The composition of claim 76, wherein R₄, R₅ and R₈ are hydrogen, R₆ and R₁₀ are hydroxyl, and Y and Z together represent trans -CH=CH-.
120. (previously presented) The composition of claim 119, wherein R₁ is methyl.
121. (previously presented) The composition of claim 88, wherein R₄, R₅ and R₈ are hydrogen, R₆ and R₁₀ are hydroxyl, and Y and Z together represent trans -CH=CH-.
122. (previously presented) The composition of claim 121, wherein R₁ is methyl.
123. (new) The composition of claim 8, wherein R₄ is hydrogen.
124. (new) The composition of claim 14, wherein R₄ is hydrogen.
125. (new) The composition of claim 82, wherein R₄ is hydrogen.
126. (new) The composition of claim 88, wherein R₄ is hydrogen.